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PHARMACOECONOMIC ASSESSMENT OF PEGASPARGASE VERSUS ASPARAGINASE IN ACUTE LYMPHOCYTIC LEUKAEMIA

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1. BACKGROUND

Acute Lymphoblastic Leukaemia (ALL) is the most commonly diagnosed neoplasia in patients under 15 years of age[1]. In Spain, the incidence rate is 1.29 per 100,000 inhabitants per year.[2]

ALL treatment is based on the administration of several drugs, but **asparaginase** is essential to the patient´s recovery.[3] **Native asparaginase** is an effective treatment for ALL, but it is associated with a high incidence of hypersensitivity reactions. When these occur, crisantaspase therapy is administered.

Pegaspargase is an asparaginase form that provides comparable efficacy to native asparaginase, with a lower administration frequency, and a decreased incidence of hypersensitivity reactions.[4,5]

The **objective** of this study was to compare the costs associated with the administration of **native asparaginase *vs.* pegaspargase** for the treatment of ALL.

2. METHODS

We carried out a **cost minimization analysis** comparing the costs of native asparaginase therapy *vs.* pegaspargase therapy, in three risk groups: standard, intermediate and high. Risk classification was based on age, patient's genetics and clinical characteristics that determine the final response to treatment. The following **two alternatives were compared**:

1. Base case (LAL/SEHOP-PETHEMA 2013 protocol[3]) therapy was as follows:

Native asparaginase was given to all patients in the induction phase, and only to standard and intermediate risk patients in the re-induction phase. High risk patients received pegaspargase in consolidation and in re-induction phases (*Table 1*).

Table 1. Number of doses administered in the base case.

RISK	PHASES			
	Induction	Consolidation	Re-induction	Maintenance
Standard	8(a)	-	4(a)	-
Intermediate	8(a)	-	4(a)	10(p)
High	8(a)	1(p) / 1(p) / 1(p)	2(p) / 2(p) / 2(p)	-

(a) Dose of native asparaginase (10,000 IU/m2, every 72h); (p) Dose of pegaspargase (1,000 IU/m2, every 14 days)

2. Alternative case (modified LAL/SEHOP-PETHEMA 2013 protocol) was as follows:

Pegaspargase replaced native asparaginase in the LAL/SEHOP-PETHEMA 2013 protocol.[3] Pegaspargase was given in the induction and the re-induction phases, keeping the rest of the treatment as in the base case (*Table 2*).

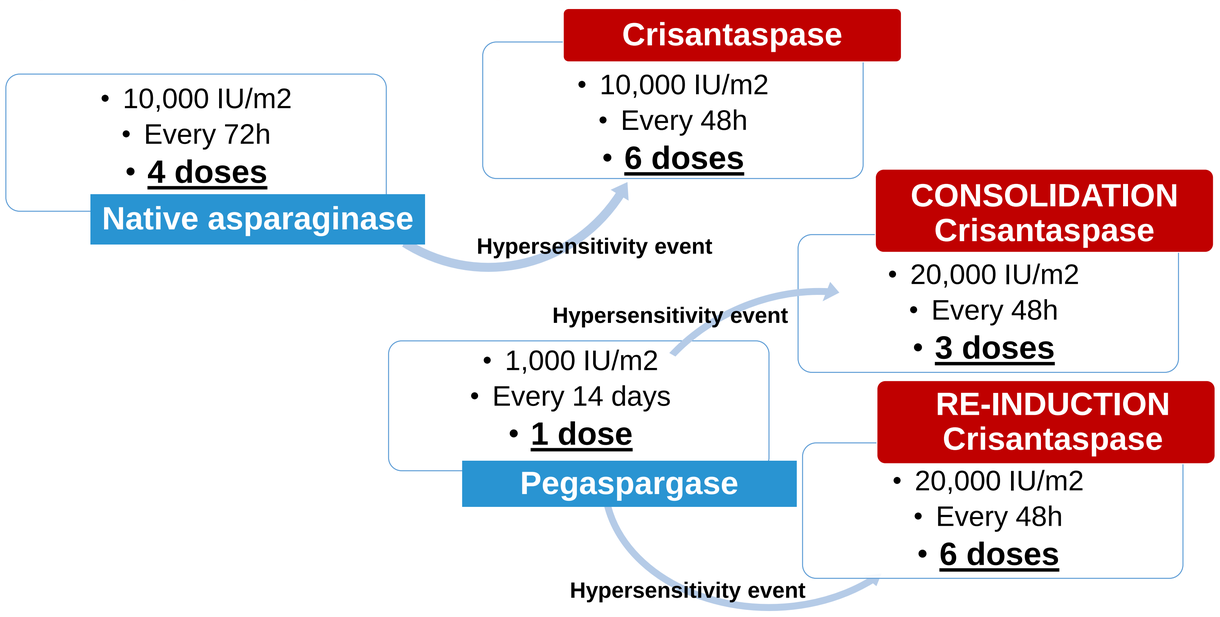
Table 2. Number of doses administered in the alternative case.

RISK	PHASES			
	Induction	Consolidation	Re-induction	Maintenance
Standard	2(p)	-	1(p)	-
Intermediate	2(p)	-	1(p)	10(p)
High	2(p)	1(p) / 1(p) / 1(p)	2(p) / 2(p) / 2(p)	-

(a) Dose of native asparaginase (10,000 IU/m2, every 72h); (p) Dose of pegaspargase (1,000 IU/m2, every 14 days)

We assumed **crisantaspase** is administered in case **of hypersensitivity reactions** with any of the compared alternatives, as indicated in Figure 1.

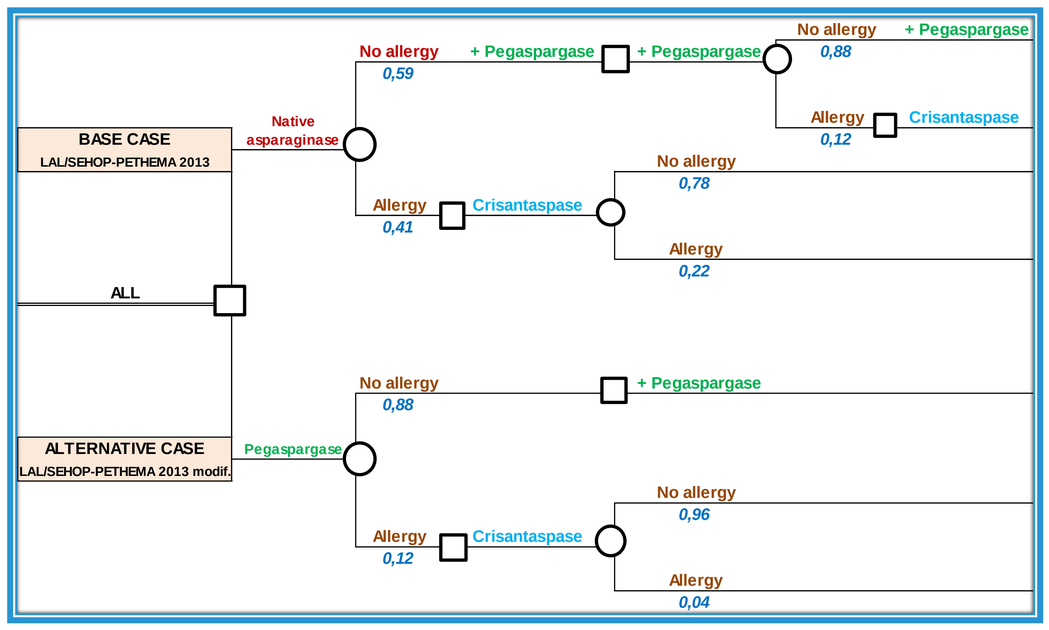
Figure 1. Proposed adjustment in asparaginase treatment.



The perspective of the model was that of the Spanish National Health System and the time horizon was 2 years. Given the perspective of the analysis, we included only direct healthcare costs: pharmaceutical costs, drug administration costs, and the cost associated with hypersensitivity events management.

A **decision tree** (Figure 2) was designed for the analysis. All transitions probabilities were taken from published clinical trials.[4-8] Probabilities of developing hypersensitivity reactions were: 41% for native asparaginase, 12% for pegaspargase,[5,6] 22% for crisantaspase in the base case, and 4% for crisantaspase in the alternative case.[7,8] All the model´s parameters were revised by an Advisory Board constituted by clinical specialists.

Figure 2. Decision tree.



Direct healthcare costs included in the model were:

- ✓ pharmaceutical costs: pegaspargase (1 vial with 3,750 IU at 1,450 €, dose 1,000 IU/m2); native asparaginase (10 vials with 10,000 IU at 528.9 €, dose 10,000 IU/m2); crisantaspase: (10,000 IU at 3,952 €, dose 20,000 IU/m2).
- ✓ drug administration: 47.5 € (Day Hospital, subsequent monitoring for early detection of hypersensitivity reaction: 1 hour).[9,10,11]
- ✓ hypersensitivity events management: 3,622 € per episode.[12]

Subgroup analysis was performed by risk category (standard 33%, intermediate 56%, and high 11%).[13,14]

3. RESULTS

Table 3 presents the results of the cost calculation.

Table 3. Cost for each analyzed scenario, by cost type and risk group.

	RISK		
	Standard	Intermediate	High
BASE CASE			
Pharmaceutical costs	1,626 €	15,724 €	17,721 €
Drug administration costs	590 €	1,046 €	932 €
Hypersensitivity events costs	2,068 €	2,068 €	2,068 €
TOTAL	**4,284 €**	**18,838 €**	**20,721 €**
ALTERNATIVE CASE			
Pharmaceutical costs	4,609 €	18,589 €	16,157 €
Drug administration costs	171 €	639 €	539 €
Hypersensitivity events costs	452 €	452 €	452 €
TOTAL	**5,232 €**	**19,680 €**	**17,148 €**

Average costs per patient are shown in *Table 4.*

Table 4. Average cost per patient.

	RISK			
	Standard	Intermediate	High	**Mean**
Base case	4,284 €	18,838 €	20,721 €	**14,243 €**
Alternative case	5,232 €	19,680 €	17,148 €	**14,634 €**

The average direct cost of pegaspargase therapy was similar to that of native asparaginase therapy (14,634 € *vs*. 14,243 € per patient), while avoiding 75 episodes of hypersensitivity in the sample population. The difference in cost per patient was 391€.

4. CONCLUSIONS

Treating naive patients diagnosed with ALL with pegaspargase instead of native asparaginase may lead to less hypersensitivity episodes, with lower administration frequency at a minimum impact in cost in Spain, improving health outcomes of patients.

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